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DATA EVALUATION RECORD

PROHEXADIONE CALCIUM TECHNICAL
(BX-112)

Study Type: §81-6; Dermal Sensitization

Work Assignment No. 1-02-25B (MRID 44457747)

Prepared for
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Disclaimer

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DATA EVALUATION RECORD

STUDY TYPE: Dermal Sensitization - Guinea pig
OPPTS Number: 870.2600 OPP Guideline Number: §81-6

DP BARCODE: D246707 SUBMISSION CODE: S543930
P.C. CODE: 112600 TOX. CHEM. NO.: None

TEST MATERIAL (PURITY): Prohexadione calcium technical (89.8% purity)

SYNONYMS: BX-112; calcium salt of 3,5-dioxo-4-propionylcyclohexane-1-carboxylic acid; KIM-112; KUH-833

CITATION: Jones, J. (1988) BX-112 technical: Buehler contact sensitisation study in the guinea pig. Safepharm Laboratories Limited, Derby, U.K. Laboratory Project Number 131/37. November 24, 1988. MRID 44457747. Unpublished.

SPONSOR: BASF Corporation, P.O. Box 13528, Research Triangle Park, NC.

EXECUTIVE SUMMARY: In a dermal sensitization study (MRID 44457747) conducted with prohexadione calcium technical (89.8% purity), 30 young adult female Dunkin-Hartley albino guinea pigs were tested using methods based on those derived by Buehler. An additional ten females were tested with 2,4-dinitrochlorobenzene and served as positive controls.

No dermal irritation was observed 24 or 48 hours following a single challenge exposure with 50% prohexadione calcium technical to either previously-induced or control animals. Acceptable positive control data were provided to validate the test methodology. Based on the results of this study, **prohexadione calcium technical is not a dermal sensitizer**.

This study is classified **acceptable (§81-6)** and satisfies the guideline requirement for a dermal sensitization study in the guinea pig.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

I. MATERIALS AND METHODS

A. MATERIALS:

1. Test Material: Prohexadione calcium technical (BX-112)
   Description: Cream-colored powder
   Lot/Batch #: G14-04
   Purity: 89.8%
   CAS #: 127277-53-6

2. Vehicle and positive control: Distilled deionized water was used as a diluent.

   The positive control portion of the study was conducted using 0.25% (w:v) and 0.1% 2,4-dinitrochlorobenzene (DNCB; purity not specified) in absolute ethanol for the induction and challenge phases, respectively.

3. Test animals: Species: Albino guinea pig
   Strain: Dunkin-Hartley
   Age: Young adult (approximately 7 to 10 weeks)
   Weight: 314-430 g (all definitive test groups)
   Source: David Hall Limited, Burton-on-Trent, Staffordshire, U.K.
   Acclimation period: ≥5 Days
   Diet: Guinea Pig FD1 Diet, Special Diet Services Limited, Wiham, Essex, U.K., ad libitum
   Water: Tap water, ad libitum
   Housing: Groups of up to four animals in solid-floor polypropylene cages
   Environmental conditions:
   Temperature: 18-23 °C
   Humidity: 60-70%
   Air changes: 15 Changes/hour
   Photoperiod: 12-Hour light/dark cycle

B. STUDY DESIGN and METHODS:

1. In-life dates: September 21 - October 29, 1988

2. Animal assignment and treatment: The study was conducted using methods derived by Buehler [Buehler, E., Archives of Dermatology, 91:171-175 (1965)]. Based on the results of a preliminary experiment conducted with two animals and prohexadione calcium technical at concentrations of 5, 10, 25, or 50% (w:w) in distilled water, a concentration of 50% was chosen for use in both phases of the definitive study.

For the induction phase, fur on the left flanks of 20 young adult female Dunkin-Hartley albino guinea pigs was clipped at an unspecified time prior to dermal administration with 0.5 mL of 50% prohexadione calcium technical for 6 hours. The test substance was applied to absorbent lint (approximately 15 x 35 mm) which was affixed to the clipped flank using Blenderm adhesive tape then covered with a strip of aluminum foil. The torso of each animal was then wrapped with Elastoplast elastic adhesive bandage. To serve as controls, an additional ten animals were treated in the same manner with 0.5 mL of distilled water. Applications were repeated twice at 7-day intervals for a total of three induction treatments. Removal of residual test material following exposure was not described.

Thirteen days following the final induction treatment, all test and control animals were subject to a single challenge exposure with 50% prohexadione calcium technical to the previously-untreated right flank and otherwise in the manner previously described. For comparison purposes, the left flank was exposed to vehicle (distilled water) only.

The guinea pigs were observed for dermal irritation approximately 24 hours after each induction application and 24 and 48 hours following the challenge treatment. Skin reactions were scored according to the following scale:

0 - No reaction
1 - Scattered mild redness
2 - Moderate and diffuse redness
3 - Intense redness and swelling

Body weights were recorded at the start (day 0) and termination (day 30) of the study. The concurrent positive control study was conducted with ten test and ten control animals and otherwise in the same manner as described for the definitive study.

II. RESULTS AND DISCUSSION:

A. Induction reactions and duration: No dermal irritation was observed during the induction phase.

B. Challenge reactions and duration: No dermal irritation was observed 24 or 48 hours following a single challenge exposure with 50% prohexadione calcium technical to either previously-induced or control animals. Based on the results of this study, prohexadione calcium technical is not a dermal sensitizer.

One animal was found dead on day 15 and another was sacrificed following discovery of a broken leg (unspecified day between days 8 and 15). No treatment-related effect on body weight was observed between animals from the test and control groups, with overall (0-30

days) average increases of 61% (n=18) and 55% (n=10), respectively.

C. Positive control: Moderate and diffuse redness (score of 2) was observed at 10/10 treatment sites 24 hours following each of the three induction treatments. In addition, small scattered scabbing was observed at 1/10 sites following the third treatment. No dermal irritation was observed during induction with vehicle (absolute ethanol) only.

Twenty-four and 48 hours following a single challenge with 0.1% DNCB to previously-induced animals, scattered mild to moderate and diffuse redness (scores of 1-2) was observed at 10/10 and 9/10 sites, respectively. In comparison, following challenge to control animals, scattered mild redness (score of 1) was observed at 1/10 sites after 24 hours. Based on the results of this study, 6/10 sites (60%) exhibited positive dermal sensitization (scores of ≥2). These data verify the adequacy of the test species and methods employed.

D. Deficiencies: It is unclear as to why the test substance was not tested at 100% (0.5 g of prohexadione calcium moistened with distilled water) in the preliminary and/or definitive studies. As a result, additional data demonstrating the dermal sensitization of prohexadione calcium technical at 100% may be requested. However, this study was deemed acceptable in demonstrating the lack of sensitization when applied according to the Buehler method at a 50% concentration.